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ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of Hodgkin's disease

Incidence

- The crude incidence of Hodgkin's disease in the European Union is 2.2/100 000 per year, the mortality 0.7/100 000 per year.

Diagnosis

- Pathological diagnosis should be made according to the World Health Organisation classification from a surgical specimen i.e. excisional lymph node biopsy, whenever possible providing enough material for fresh, frozen and formalin-fixed samples.
- Classical Hodgkin's disease (cHD) includes nodular sclerosing, mixed cellularity, lymphocyte-rich classical and lymphocyte-depleted subtypes and is distinguished from lymphocyte-predominant Hodgkin's disease (LPHD) for prognostic reasons.

Staging and risk assessment

- Chest X-ray and a CT-scan of the chest and abdomen, and a bone marrow biopsy are mandatory.
- Staging laparotomy is not recommended *[II, A]*. As an option, PET-scan may be considered in addition to the CT-scan.
- Full blood count, ESR, and blood chemistry including C-reactive protein, alkaline phosphatase, albumin, and LDH *[II–III, A]*.
- The staging according to the Ann. Arbor system with mentioning of B-symptoms, bulky disease, involvement of the spleen and extranodal sites is mandatory for evaluation of the risk for relapse and for choosing the correct treatment.
- Risk assessment is recommended according to the categories shown in Table 1 *[II–III, A]*.

Treatment plan

- ***Note***: LPHD is an indolent disease with a tendency to recur. LPHD stage I disease may be treated with involved field irradiation (30 Gy) only. For recurrent disease aggressive therapy should be avoided. Rituximab is an option.
- For all other patients a multidisciplinary treatment planning should be established. The following treatment recommendations apply to patients able to tolerate anthracycline therapy.

Limited stage patients

- 2–4 cycles of ABVD (or an equivalent regimen) are used in combination with involved field radiotherapy (30–36 Gy).

Intermediate stage patients

- Four cycles of ABVD (or an equivalent regime) combined with involved field irradiation (30–36 Gy) *[I, A]*.

Advanced stage patients

- Eight cycles of ABVD (or BEACOPP). Involved field radiotherapy (30–36 Gy) should be applied only to initially bulky tumors (> 7.5 cm) or to sites of residual disease after chemotherapy *[I–II, A]*. The probable superiority of escalated BEACOPP over ABVD for advanced stages still requires long-term confirmation from ongoing randomized trials.

Response evaluation

- To be done after 4 cycles and after the last cycle of chemo- or chemo-/radiotherapy by physical examination, laboratory analysis as above, and the same initially abnormal radiographic tests. Patients with incomplete radiological response should be evaluated for active disease by biopsy or at least by repeat radiological testing. If available, PET-scan may identify partial responders at high risk for early relapse *[III, B]*.

Follow-up

- History and physical exam every 3 months for 1 year, every 6 months for 3 years, then once a year *[V, D]*.
- Laboratory analysis as above and chest X-ray at 6, 12, and 24 months, then as clinically needed in patients suitable for further therapy *[V, D]*.
- CT-scan and repetition of initially pathologic radiographic tests once to confirm remission status. Further regular CT-scans are not recommended except for evaluation of residual disease.
- Evaluation of thyroid function (TSH) in patients with irradiation to the neck at 1, 2, and at least at 5 years *[III, A]*.
- After chest irradiation at premenopausal age, especially at an age below 25 years, women should be screened for

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Table 1.

Limited stage	Clinical Stage (CS) I and II without risk factors
Intermediate stage	CS I or II with one or more of the following risk factors: –large mediastinal mass (>1/3 of thoracic width on chest X-ray, >7.5 cm in CT-scan) –extranodal involvement –massive involvement of the spleen (diffuse enlargement or > 5 nodules) –elevated ESR (>30 mm/h for B-stages or >50 mm/h for A-stages) –extensive lymph node involvement (≥3 lymph node areas) –older age (>60 years) may be an additional risk factor
Advanced stage	CS III or IV

secondary breast cancers clinically *[III, A]* and, after the age of 40–50 years, by mammography *[III, C]*.

Treatment of Hodgkin's disease relapsing after chemotherapy

- Salvage therapy with e.g. DHAP, EPOCH, or Dexa-BEAM is indicated. If the disease remains chemosensitive, stem cell collection, high-dose chemotherapy and autologous stem cell transplantation is indicated for patients with good performance status.
- Low-intensity treatment including novel single agents and/or regional radiotherapy may offer good quality of life for the remaining patients.

Note

Levels of Evidence *[I–V]* and Grades of Recommendation *[A–D]* as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

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